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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/587,771	07/28/2006	Robert W. Marquis JR.	PU60731	1281

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SMITHKLINE BEECHAM CORPORATION  
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KING OF PRUSSIA, PA 19406-0939

EXAMINER
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OH, TAYLOR V

ART UNIT	PAPER NUMBER
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1625

NOTIFICATION DATE	DELIVERY MODE
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09/23/2008

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

US\_cipkop@gsk.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/587,771	<b>Applicant(s)</b> MARQUIS ET AL.	
	<b>Examiner</b> Taylor Victor Oh	<b>Art Unit</b> 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 28 July 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-11 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>7/28/06</u>   | 6) <input type="checkbox"/> Other: _____                          |

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The Status of Claims:

Claims 1-11 are pending.

Claims 1-11 are rejected.

DETAILED ACTION

1. Claims 1-11 are under consideration in this Office Action.

Priority

2. It is noted that this application is a 371 of PCT/US05/03499 (02/04/2005 which claims benefit of 60/542,554(02/06/2004).

Drawings

3. None.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, the term "substituted " is recited.

This expression is vague and indefinite because in the absence of the specific moieties intended to effectuate modification by the “substitution” or attachment to the chemical core claimed, the term “substituted” renders the claims in which it appears indefinite in all occurrences wherein applicants fails to articulate by chemical name, structural formula or sufficiently distinct functional language, the particular moieties applicants regards as those which will facilitate substitution, requisite to identifying the composition of matter claimed.

Appropriate correction is required.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated clearly by Lago et al (WO 01/53254A).

Lago et al discloses the following compounds (see page 9, lines 25-30):

4-{3-Cyano-4-[(R)-3-(1,1-dimethyl-2-naphthalen-2-yl-ethylamino)-2-hydroxy-propoxy]-phenyl}-butyric acid;  
3-{2-Cyano-3-[(R)-3-(2-indan-2-yl-1,1-dimethyl-ethylamino)-2-hydroxy-propoxy]-phenyl}-propionic acid ethyl ester;  
4-{2-Cyano-3-[(R)-3-(2-indan-2-yl-1,1-dimethyl-ethylamino)-2-hydroxy-propoxy]-phenyl}-butyric acid ethyl ester;

***Claim Rejections - 35 USC § 103***

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

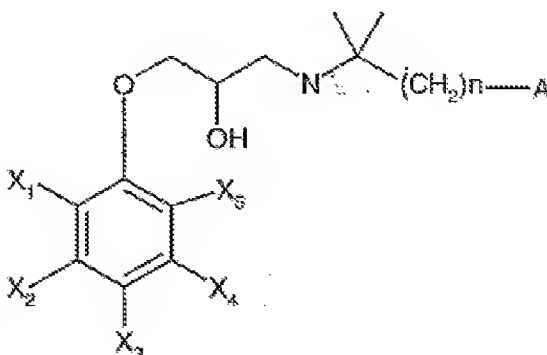
The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lago et al (WO 01/53254A).

Lago et al discloses the followings(see page 2 ,lines 25-30).

The present invention comprises novel calcium receptor antagonists represented by Formula (I) hereinbelow and their use as calcium receptor antagonists in the treatment of a variety of diseases associated with abnormal bone or mineral homeostasis, including but not limited to hypoparathyroidism, osteosarcoma, periodontal disease, fracture healing, osteoarthritis, rheumatoid arthritis, Paget's disease, humoral hypercalcemia associated with malignancy and fracture healing, and osteoporosis.



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wherein:

A is an aryl or fused aryl, dihydro or tetrahydro fused aryl, heteroaryl or fused heteroaryl, dihydro or tetrahydro fused heteroaryl, unsubstituted or substituted with any substituent being selected from the group consisting of halogen, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, CF<sub>3</sub>, and OCF<sub>3</sub>;

X<sub>1</sub> and X<sub>5</sub> are independently selected from the group consisting of H, halogen, CN, and NO<sub>2</sub>, provided that either X<sub>1</sub> or X<sub>5</sub> is H;

X<sub>2</sub>, X<sub>3</sub> and X<sub>4</sub> are selected from the group consisting of H, halogen, O-C<sub>1-4</sub> alkyl, and J-K, wherein:

J is a covalent bond, alkylene, O-alkylene or alkenylene;

K is selected from the group consisting of, CO<sub>2</sub>R<sub>5</sub>, CONR<sub>4</sub>R'<sub>4</sub>, and NR<sub>4</sub>R'<sub>4</sub>;

R<sub>4</sub> and R'<sub>4</sub> are independently H, alkyl, aryl or heteroaryl;

R<sub>5</sub> is H, alkyl, or alkyl-(O-alkyl)<sub>m</sub>-O-alkyl;

n is an integer from 0 to 4; and

m is an integer from 1-3.

(see page 4 ,lines 10-25).

The following compounds are exemplified as below:(see page 9, lines 25-30):

4-{3-Cyano-4-[(R)-3-(1,1-dimethyl-2-naphthalen-2-yl-ethylamino)-2-hydroxy-propoxy]-phenyl}-butyric acid;

3-{2-Cyano-3-[(R)-3-(2-indan-2-yl-1,1-dimethyl-ethylamino)-2-hydroxy-propoxy]-phenyl}-propionic acid ethyl ester;

4-{2-Cyano-3-[(R)-3-(2-indan-2-yl-1,1-dimethyl-ethylamino)-2-hydroxy-propoxy]-phenyl}-butyric acid ethyl ester;

In a preferred embodiment of the present invention, the present compound is co-administered with an anti-resorptive agent. Suitable anti-resorptive agents for co-administration include, but are not limited to estrogen, 1, 25 (OH)<sub>2</sub> vitamin D<sub>3</sub>, calcitonin, selective estrogen receptor modulators, vitronectin receptor antagonists, V-H<sup>+</sup>-ATPase inhibitors, src SH<sub>2</sub> antagonists, bisphosphonates and cathepsin K inhibitors.

(see page 18, lines 23-25):

The instant invention, however, differs from the prior art in that the claimed compound is

4-{3-Cyano-2-[(R)-2-hydroxy-3-(2-indan-2-yl-1,1-dimethyl-ethylamino)-propoxy]-phenyl}-butyric acid ethyl ester.

Even so, the prior art discloses a similar compound (see page 9, lines 29-30):

4-{2-Cyano-3-[(R)-3-(2-indan-2-yl-1,1-dimethyl-ethylamino)-2-hydroxy-propoxy]-phenyl}-butyric acid ethyl ester;

They are in a relationship of positional isomers. It is well established that position isomers are prima facie structurally obvious even in the absence of a teaching to modify. The isomer is expected to be prepared by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing the position isomers. This circumstance has arisen many times.

See: *Ex parte Englehardt*, 208 USPQ 343, 349; *In re Mehta*, 146 USPQ 284, 287; *In re Surrey*, 138 USPQ 67; *Ex Parte Ulliyot*, 103 USPQ 185; *In re Norris*, 84 USPQ 459; *Ex Parte Naito*, 168 USPQ 437, 439; *Ex parte Allais*, 152 USPQ 66;



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*In re Wilder*, 166 USPQ 545, 548; *Ex parte Henkel*, 130 USPQ 474; *Ex parte Biel*, 124 USPQ 109; *In re Petrzilka*, 165 USPQ 327; *In re Crownse*, 150 USPQ 554; *In re Fouche*, 169 USPQ 431; *Ex parte Ruddy*, 121 USPQ 427; *In re Wiechert*, 152 USPQ 249, *In re Shetty*, 195 USPQ 753.

For example, “Position isomerism has been used as a tool to obtain new and useful drugs” (Englehardt) and “Position isomerism is a fact of close structural similarity” (Mehta, emphasis in the original). See also MPEP 2144.09, second paragraph.

Therefore, it would have been obvious to the skilled artisan in the art to be motivated to prepare the position isomers as an alternative due to their structural similarity. This is because the isomer is expected to be prepared by the same method and to have generally the same properties.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taylor Victor Oh whose telephone number is 571-272-0689. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner’s supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Taylor Victor Oh, MSD,LAC  
Primary Examiner  
Art Unit :1625

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Primary Examiner, Art Unit 1625  
8/29/08